[CONTRIBUTION FROM THE WILLIAM H. NICHOLS LABORATORY, NEW YORK UNIVERSITY]

PREPARATION AND HYDROGENATION OF 2-SUBSTITUTED 4,7-PHENANTHROLINES

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Only one preparation of 4,7-phenanthrolines carrying 2-alkyl or 2-aryl substituents has been reported (1). We have devised a method whereby certain of these compounds may be synthesized, and have studied the hydrogenation of several of them.

The starting compound for these syntheses, 6-aminoquinoline (I), was prepared conveniently by the Raney nickel reduction of 6-nitroquinoline. The reduction of this compound to the amine has been accomplished by several methods (2–4), but apparently never by Raney nickel, although the latter has been employed to produce the 5- and 7-aminoquinoline isomers (5). We have found that the use of Raney nickel, like that of palladium on calcium carbonate (4), prevents formation of troublesome by-products.

6-Aminoquinoline was then condensed with substituted ethyl malonates under conditions essentially similar to those used by Baker (6) in his modification of Baumgarten's synthesis of substituted quinolines (7). Approximately equimolar amounts of the substituted ethyl malonates and the amine were heated in a diphenyl ether solution to 220–250°. High yields of the 2-substituted 1,3-dihydroxy-4,7-phenanthrolines (II) were thus obtained. The course of this reaction could conveniently be followed by measuring the volume of ethanol evolved. The 2-ethyl-, 2-methyl-, and 2-phenyl-1,3-dihydroxy-4,7-phenanthrolines melted above 360° and were insoluble in water and organic solvents. They were consequently used in the next step of the synthesis without further purification. The 2-benzyl derivative, however, could be purified by recrystallization from ethanol. It gave a negative ferric chloride test and was insoluble in strong aqueous bases. The possibility of its being a stericly hindered true phenol appears slight; the hydroxyl groups *alpha* and *gamma* to the ring nitrogen are not phenolic in pyridine (8) or in quinoline (9). It has been suggested (10) that 2- and 4-hydroxypyridines may exist principally as resonance hybrids of the lactam and zwitterion forms. The ultraviolet absorption spectrum of 1,3-dihydroxy-2-benzyl-4,7-phenanthroline (Figure 1) is not in conflict with that concept; furthermore, the high melting points and low solubilities of the 1,3-dihydroxy-4,7-phenanthrolines we have prepared are consistent with the properties of zwitterions.

Refluxing II with phosphorus oxychloride resulted in high yields of the 1,3-dichloro-4,7-phenanthrolines (III), which could be purified by recrystallization from ethanol or benzene. The ultraviolet absorption spectrum of the 2-methyl derivative is shown in Figure 1.

It had been thought that 1,3-dihydroxy- and 1,3-dichloro-4,7-phenanthroline themselves (II and III, R = H) might be obtained through cyclization of the

malonic acid monoamide of 6-aminoquinoline (V). This latter substance was easily prepared by heating the amine with ethyl malonate and hydrolyzing the resulting monoamide ester (IV); but heating V with such agents as concentrated sulfuric acid, phosphorus oxychloride, phosphorus pentachloride, and zinc chloride in various solvents did not bring about cyclization. Heating alone above 170° decarboxylated the compound to give 6-acetylaminoquinoline.

Attempts were made to replace the chlorine atoms in III by hydrogenation in an absolute ethanolic solution in the presence of Raney nickel and sodium ethoxide. Reduction was interrupted when two mole-equivalents of hydrogen had been adsorbed. The 2-methyl and 2-ethyl derivatives produced complex mixtures from which none of the desired products could be isolated. However,

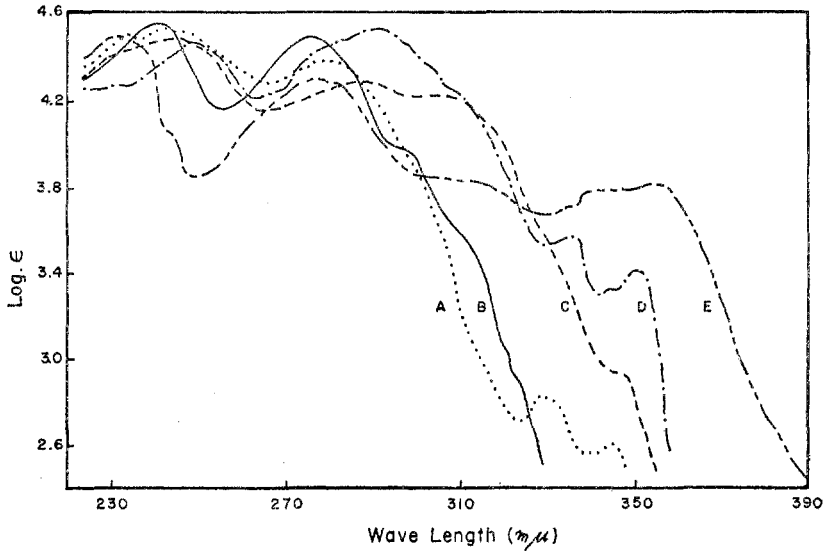
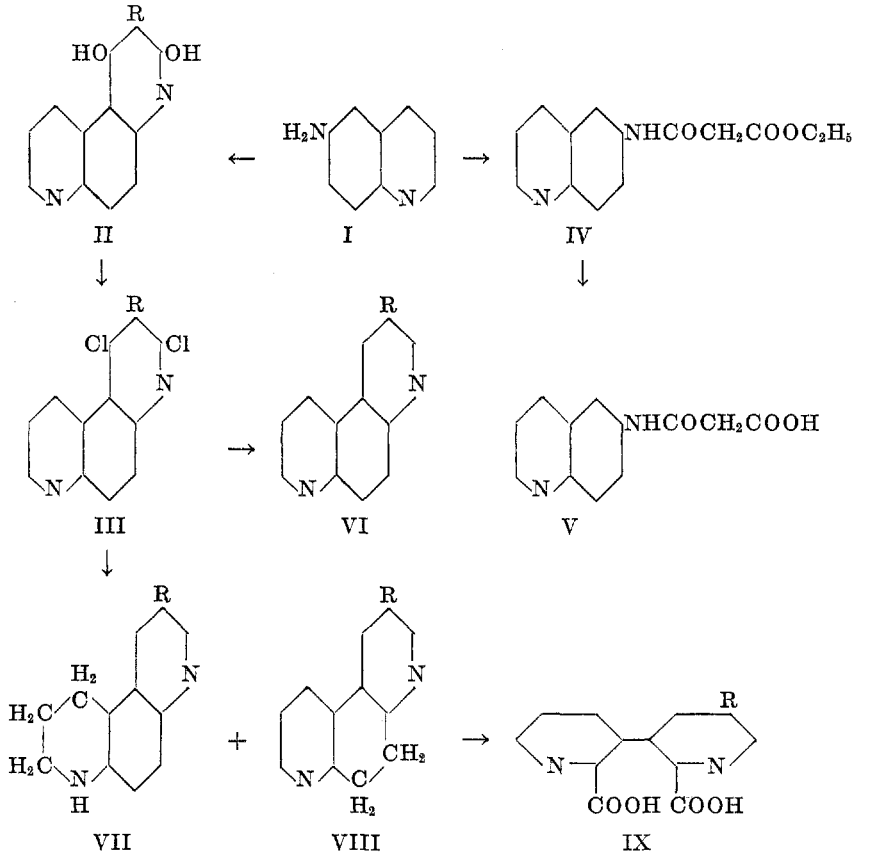


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA IN 95% ETHANOL: A, 1,3-dichloro-2-methyl-4,7-phenanthroline; B, 2-benzyl-4,7-phenanthroline; C, 2-phenyl-4,7-phenanthroline; D, 3-phenyl-4,7-phenanthroline; E, 1,3-dihydroxy-2-benzyl-4,7-phenanthroline.

hydrogenation of the 2-phenyl and 2-benzyl derivatives gave the corresponding 4,7-phenanthrolines (VI). The ultraviolet absorption spectra of these compounds are given in Figure 1. For comparison purposes the spectrum of 3-phenyl-4,7-phenanthroline, which has previously been prepared (5), was determined and is also included.

When the hydrogenation of III was not interrupted, the pressure of the system continued falling until approximately three equivalents of hydrogen had been absorbed. The methyl-, ethyl-, and benzyl-substituted compounds each gave a mixture of two chlorine-free products. Neither of the two benzyl derivatives was 2-benzyl-4,7-phenanthroline. The higher-melting member of each pair was yellow, had the lower solubility in organic solvents, and formed a white acetyl derivative. The lower-melting member was white or colorless and formed

no acetyl derivative. Hydrogenation of 1,3-dichloro-2-phenyl-4,7-phenanthroline gave a white, chlorine-free compound which was not 2-phenyl-4,7-phenanthroline and which formed no acetyl derivative, and an orange tar from which no crystalline substance could be isolated.



In order to clarify the course of this reaction, 4,7-phenanthroline itself was prepared by a Skraup synthesis on *p*-phenylenediamine as described by Smith (11). This compound was hydrogenated under the conditions described above. Two substances were also obtained in this way. The lower-melting one was white and formed no acetyl derivative. The less-soluble, higher-melting compound had the yellow color and the melting point reported by Matsumura (12) for 1,2,3,4-tetrahydro-4,7-phenanthroline; its acetyl derivative was prepared in the manner described by Wibaut (13) and had the same melting point he reported. These data, in conjunction with analyses, indicated that the yellow solids we had produced were tetrahydro-4,7-phenanthrolines (VII). The conclusion as to common structure was confirmed by the close similarities among their ultraviolet absorption spectra (Figure 2).

Ochiai and Kuroyanagi (14) have prepared a yellow tetrahydro derivative by

reducing 1,3-dimethyl-4,7-phenanthroline with tin and hydrochloric acid, assigning to it the structure 7,8,9,10-tetrahydro-1,3-dimethyl-4,7-phenanthroline by analogy with the hydrogenation of 2,4-dimethylquinoline to yield a 5,6,7,8-tetrahydro derivative. They further state that a methyl radical on a pyridine nucleus in 4,7-phenanthroline prevents hydrogenation of that nucleus, citing as reason for this conclusion the hydrogenation of comparably substituted quinolines and naphthyridines. We did not consider such evidence alone as reliable, however, since several reports of quinolines substituted with methyl groups on the pyridine nucleus yielding 1,2,3,4-tetrahydro products are extant (15). In order to determine whether the substituted or the unsubstituted pyridine rings of the above tetrahydro-4,7-phenanthrolines had been hydrogenated, one of them was oxidized with alkaline potassium permanganate. In this way VII

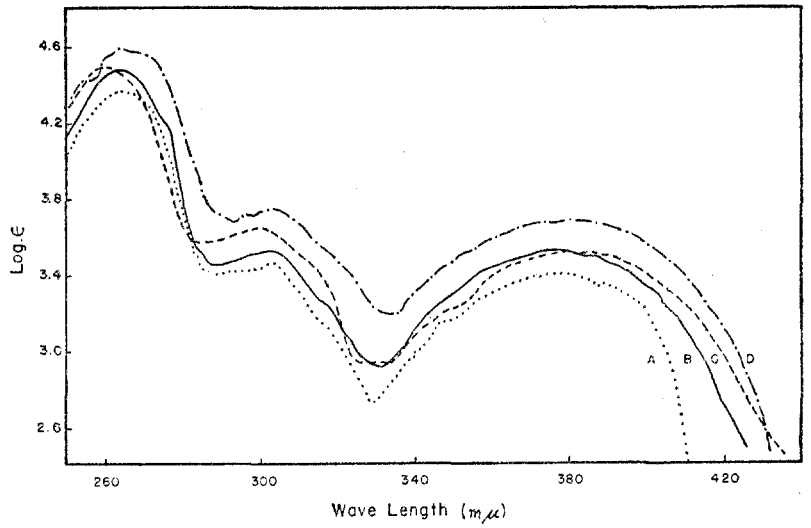


FIG. 2. ULTRAVIOLET ABSORPTION SPECTRA IN 95% ETHANOL of tetrahydro-4,7-phenanthroline (C) and some 2-substituted derivatives: 2-methyl- (A); 2-ethyl- (B); and 2-benzyl (D).

(R = CH_3) gave 2,3,5-tricarboxypyridine, indicating that hydrogenation had indeed occurred in the unsubstituted pyridine nucleus. (Had the reverse proved true, the isolation of quinolinic acid would have been expected.) The identity of this degradation product was confirmed by its conversion into a known derivative, 3,5-dicarbomethoxypyridine.

The white hydrogenation products of 4,7-phenanthroline and the 2-substituted 4,7-phenanthrolines formed no acetyl derivatives, showing that the benzene rather than a pyridine ring had been reduced. The stoichiometry of the hydrogenation suggested that they were dihydro derivatives. These facts indicated that the reduction products were 5,6-dihydro-4,7-phenanthrolines (VIII). (The ultraviolet absorption spectra of 5,6-dihydro-4,7-phenanthroline and its 2-benzyl analog are given in Figure 3.)

Confirmation of this conclusion was afforded by their oxidation. Previous workers (3, 11) have reported that oxidation of 4,7-phenanthroline with alkaline

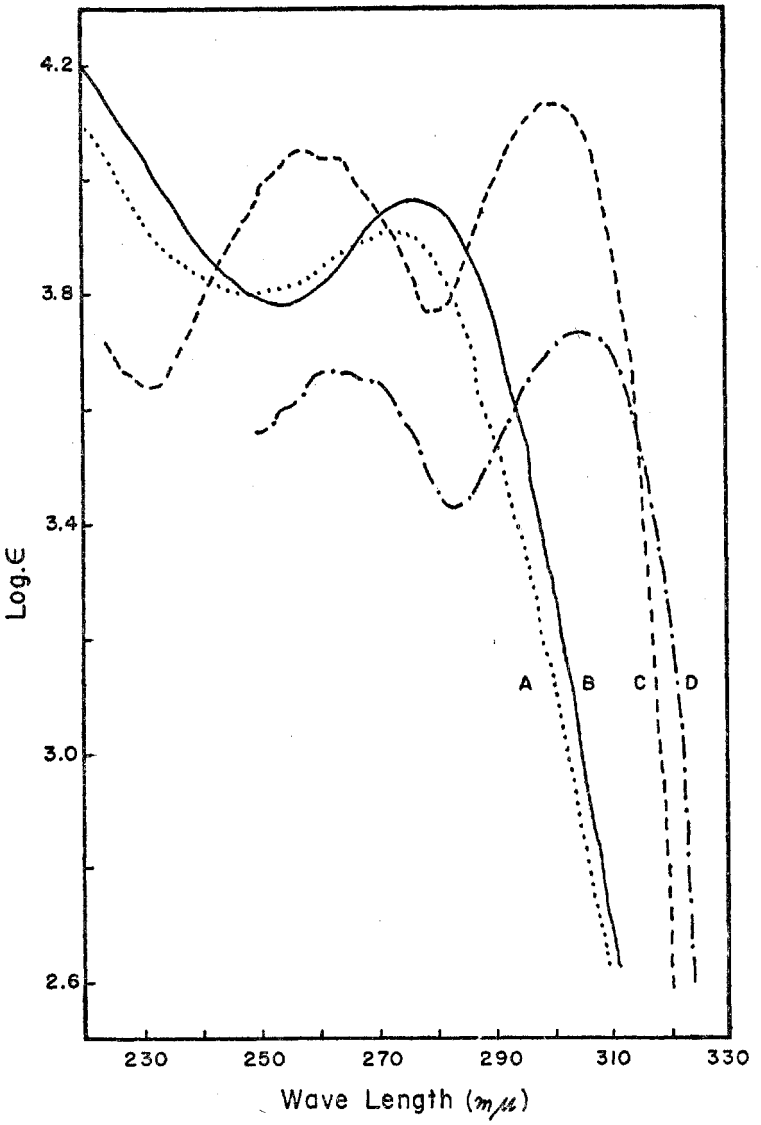


FIG. 3. ULTRAVIOLET ABSORPTION SPECTRA IN WATER: A, 3,3′-bipyridyl-2,2′-dicarboxylic acid; B, 5-methyl-3,3′-bipyridyl-2,2′-dicarboxylic acid; IN 95% ETHANOL: C, 5,6-dihydro-4,7-phenanthroline; D, 2-benzyl-5,6-dihydro-4,7-phenanthroline.

permanganate produced 2,2′-dicarboxy-3,3′-bipyridyl. We found that 5,6-dihydro-4,7-phenanthroline under similar treatment led to the formation of the same product. Likewise, oxidation of the phenyl, methyl, and benzyl derivatives

of VIII produced the corresponding 5-substituted 2,2′-dicarboxy-3,3′-bipyridyls (IX). The ultraviolet absorption spectra of two of these compounds are given in Figure 3.

EXPERIMENTAL

6-Aminoquinoline. 6-Nitroquinoline (15.0 g., 0.086 mole) was suspended in 200 ml. of absolute ethanol; W-2 Raney nickel sludge (2 ml.) was added, and the suspension was shaken at room temperature in a hydrogen atmosphere under an initial pressure of 50 p.s.i. After nine hours, three mole-equivalents of hydrogen had been absorbed. The catalyst was filtered off immediately, and as the filtrate darkened rapidly on exposure to air, a concentrated alcoholic solution of hydrogen chloride was added at once to precipitate the stable dihydrochloride. The yellow solid thus obtained was filtered from the solution, washed with ethanol, and vacuum-dried. It was dissolved in 150 ml. of water and refluxed one hour with Norit (charcoal). The solution was filtered and cooled, and the free base was regenerated by the addition of an aqueous sodium hydroxide solution. The white 6-aminoquinoline separated as a quickly-solidifying oil and was filtered from the solution, washed with water, and vacuum-dried. The product (m.p. 115–116°) weighed 10.5 g. (85% yield).

Ethyl-N-(6-quinolyl)malonamate. A solution of 11.5 g. (0.080 mole) of 6-aminoquinoline and 38.0 g. (0.237 mole) of ethyl malonate in 150 ml. of xylene was refluxed for 90 minutes. The dark solution was cooled in an ice-bath for 30 minutes, then decanted from the red tar which had formed on the bottom and sides of the flask. The solution was refluxed 30 minutes with Norit. On filtering and then cooling a portion of this solution in an ice-methanol bath at −15°, white crystals were obtained. The main bulk of the solution was then cooled in an ice-bath and seeded with these crystals. After several days' refrigeration, the precipitate which had formed was filtered from the solution, washed three times with petroleum ether, and air-dried. The solid weighed 11.5 g. (56% yield) and melted at 123–126°. Two recrystallizations from a benzene-ligroin solution gave white, fibrous crystals melting at 131–133°.

Anal. Calc'd for $C_{14}H_{14}N_2O_3$: N, 10.85. Found: N, 10.58.

N-(6-quinolyl)malonamic acid. Ethyl N-(6-quinolyl)malonamate (5.6 g., 0.0217 mole) was added to a solution of sodium bicarbonate (6.3 g.) in water (60 ml.). The suspension was stirred vigorously and heated in a boiling water-bath. The emulsion which formed initially disappeared within 20 minutes. After one hour the solution was evaporated to 30 ml. It was then cooled, made just acid to Congo Red with hydrochloric acid, and refrigerated overnight. The yellow solid which precipitated was washed with water and vacuum-dried. This substance weighed 4.5 g. (90% yield), and was in the form of micro-crystals, m.p. 174–176° with decomposition. After recrystallization from water these melted at 168° with decomposition.

Anal. Calc'd for $C_{12}H_{10}N_2O_3$: N, 12.18. Found: N, 12.36.

1,3-Dihydroxy-2-benzyl-4,7-phenanthroline. Ethyl benzylmalonate (13.3 g., 0.0530 mole), 6-aminoquinoline (7.00 g., 0.0486 mole), and diphenyl ether (21 ml.) were placed in a flask equipped with a ground glass neck. A reflux condenser was fitted in place, and the flask was placed in a metal bath at 220°. Steam was passed through the condenser jacket. The products which were still gaseous were led from the top of the first condenser into a tilted second one which was cooled by cold water. A liquid, identified as ethanol, condensed in the latter and was collected. Over a 45-minute period the bath temperature was gradually raised to 260°, at which point it was held for an additional 30 minutes. During the entire heating period 4.9 ml. (0.084 mole) of ethanol distilled from the system. The reaction mixture was then cooled and filtered. The residue, a red-brown powder, was first washed with ligroin, and then acetone. This crude 1,3-dihydroxy-2-benzyl-4,7-phenanthroline weighed 12.0 g. (82% yield). Slender white crystals melting at 302–305° were obtained after three crystallizations from ethanol.

Anal. Calc'd for $C_{19}H_{14}N_2O_2$: N, 9.27. Found: N, 9.34.

The *picrate* formed yellow rhombic crystals from ethanol, m.p. 250–253° with decomposition.

1,3-Dichloro-2-benzyl-4,7-phenanthroline. A suspension of crude 1,3-dihydroxy-2-benzyl-4,7-phenanthroline (11.0 g., 0.0364 mole) in phosphorus oxychloride (45 ml.) was refluxed for 75 minutes. The reaction mixture was cooled, and then poured over about 400 g. of crushed ice. Concentrated aqueous ammonia was added until the suspension was alkaline, and the resulting brown precipitate was filtered from the solution, washed with water, and vacuum-dried. It was refluxed with 150 ml. of benzene for one hour, filtered hot, and the solution then was refluxed with 2 g. of Norit for 30 minutes. The solution was filtered, evaporated to 20 ml., and 80 ml. of absolute ethanol was added. After overnight refrigeration, the crystals which had formed were filtered off and air-dried. This product weighed 8.60 g. (70% yield) and melted at 128–131°. After recrystallizing three times from ethanol, white needles (m.p. 144.5–146°) were obtained.

Anal. Calc'd for $C_{19}H_{12}Cl_2N_2$: N, 8.26. Found: N, 8.30.

The *picrate* formed yellow needles from ethanol, m.p. 243–246° with decomposition.

1,3-Dichloro-2-methyl-4,7-phenanthroline. Uncrystallized 1,3-dihydroxy-2-methyl-4,7-phenanthroline (prepared in 88% yield from ethyl methylmalonate and 6-aminoquinoline in the manner previously described) was added to phosphorus oxychloride and the resulting mixture was treated as described above. The product, obtained in 61% yield, was collected as feathery, white needles of m.p. 177.5–179.5° after two recrystallizations from ethanol.

Anal. Calc'd for $C_{13}H_8Cl_2N_2$: N, 10.65. Found: N, 10.38.

The *picrate* formed slender yellow needles from ethanol, m.p. 174–177°.

1,3-Dichloro-2-phenyl-4,7-phenanthroline. Uncrystallized 1,3-dihydroxy-2-phenyl-4,7-phenanthroline (prepared in 90% yield from ethyl phenylmalonate and 6-aminoquinoline) was added to phosphorus oxychloride and the resulting mixture was treated as described above. The product was obtained in 88% yield, and formed white needles of m.p. 264–265° after recrystallization from benzene.

Anal. Calc'd for $C_{18}H_{10}Cl_2N_2$: N, 8.62. Found: N, 8.60.

The *picrate* formed slender yellow needles from ethanol, m.p. 211–214° with decomposition.

1,3-Dichloro-2-ethyl-4,7-phenanthroline. Uncrystallized 1,3-dihydroxy-2-ethyl-4,7-phenanthroline (prepared in 81% yield from ethyl ethylmalonate and 6-aminoquinoline) was added to phosphorus oxychloride and the resulting mixture was treated as described above. The product was obtained in 74% yield. It was best purified for analysis by dissolving a small portion in absolute ethanol and adding a few drops of sulfuric acid. The resulting sulfate was recrystallized twice from absolute ethanol. The free base was precipitated from an aqueous solution of the sulfate by ammonia, and then again recrystallized from absolute ethanol. White needles of m.p. 159.5–161° were obtained in this manner.

Anal. Calc'd for $C_{14}H_{10}Cl_2N_2$: N, 10.11. Found: N, 10.30.

The *picrate* formed yellow cubes from ethanol, m.p. 225–228°.

2-Phenyl-4,7-phenanthroline. Sodium (2.5 g., 0.11 mole) was dissolved in 200 ml. of absolute ethanol. 1,3-Dichloro-2-phenyl-4,7-phenanthroline (12.0 g., 0.0369 mole) was added, followed by 2 ml. of a W-2 Raney nickel-alcohol sludge. The suspension was shaken in an atmosphere of hydrogen under an initial pressure of 34 p.s.i. After 5.5 hours two mole-equivalents of hydrogen had been absorbed. At this point the nickel and sodium chloride were removed by filtration, and the solution was made exactly neutral by the careful addition of hydrochloric acid. The sodium chloride was then filtered off and the solution evaporated to dryness. The residue, which was a brittle red tar, was dissolved in 100 ml. of ethyl acetate and refluxed with 1 g. of Norit for one hour. After filtering, the solution was evaporated to 15 ml. and 25 ml. of isopropyl ether was added. Seed crystals were obtained by placing a few ml. in a Dry Ice-acetone bath. These were added to the main bulk of the solution, which was then refrigerated overnight. After being filtered and washed with isopropyl ether, the air-dried light yellow fibers weighed 4.6 g. (49% yield) and melted at 130–140°.

The analytical sample was purified by transforming it to the sulfate and recrystallizing it twice from absolute ethanol. After regeneration, the free base was recrystallized from isopropyl ether. Fine white needles melting at 152–153.5° were obtained in this fashion.

Anal. Calc'd for $C_{18}H_{12}N_2$: N, 10.93; C, 84.35; H, 4.72.

Found: N, 11.12; C, 83.87; H, 5.02.

The *picrate* formed slender yellow needles from ethanol, m.p. 262–265°.

2-Benzyl-4,7-phenanthroline. Sodium (2.5 g., 0.11 mole) was dissolved in 200 ml. of absolute ethanol. 1,3-Dichloro-2-benzyl-4,7-phenanthroline (10.0 g., 0.0295 mole) was added, followed by 2 ml. of Raney nickel. The suspension was shaken in an atmosphere of hydrogen under an initial pressure of 34 p.s.i. After 8 hours two mole-equivalents of hydrogen had been absorbed. The solids were filtered off, and the solution was made just neutral by the careful addition of concentrated hydrochloric acid. After filtering again, the solution was heated on a steam-bath. A hot solution of 16 g. of picric acid in 400 ml. of 95% ethanol was added. After being refrigerated overnight, the yellow picrate which had precipitated was filtered off and recrystallized from 95% ethanol (2 l.). The 7.0 g. of picrate obtained after filtering and vacuum-drying was placed in a water solution (400 ml.) of sodium hydroxide (5 g.), and extracted three times with 150-ml. portions of ether. The combined ethereal extracts were washed with water, dried over sodium sulfate, and evaporated to 50 ml. After overnight refrigeration, the white plates which had precipitated were filtered off and air-dried; they weighed 2.38 g. and melted at 132–135°. By successive evaporation and refrigeration of the mother liquor an additional quantity of a less pure product was obtained. The total yield was 2.68 g. (34%). White slender plates melting at 138–140° were formed after two recrystallizations from ether.

Anal. Calc'd for $C_{19}H_{14}N_2$: N, 10.37. Found: N, 10.64.

The *picrate* formed yellow needles from ethanol, m.p. 200–204°.

1,2,3,4-Tetrahydro-4,7-phenanthroline. Sodium (1.0 g.) was dissolved in 200 ml. of absolute ethanol. 4,7-Phenanthroline (6.8 g., 0.0378 mole) was added, followed by 2 ml. of Raney nickel sludge. The suspension was shaken in an atmosphere of hydrogen under an initial pressure of 54 p.s.i. After 6 hours 1.5 mole-equivalents of hydrogen had been absorbed; shaking another hour did not result in any further pressure drop. The nickel was filtered off, and the solution was made exactly neutral by the careful addition of concentrated hydrochloric acid. After filtering, the ethanol was evaporated by boiling, the volume of the solution being kept constant by the addition of water, until the temperature of the escaping vapor indicated that the solution was about 10% ethanol. The solution was refrigerated overnight, and the precipitated yellow solid was filtered off, washed with 10% aqueous ethanol (the washings being added to the filtrate, which was set aside for later use) and vacuum-dried. A yield of 2.7 g. (40%) was obtained, m.p. 141–150°. After two recrystallizations from benzene, yellow rhombic crystals were obtained which melted at 152.5–154°, compared to 152–152.5° reported by Matsumura (12).

The *acetyl derivative* was prepared by the method of Wibaut (13). After recrystallization from ethanol slender white rods were obtained, m.p. 120–120.5°. (Wibaut reported 121°.)

5,6-Dihydro-4,7-phenanthroline. The dihydro derivative was produced concurrently with the tetrahydro derivative by the above-described hydrogenation. The combined filtrate and washings obtained after separation of the tetrahydro compound were boiled, keeping the volume constant by the addition of water, until the temperature of the escaping vapor indicated that ethanol was absent. The solution was cooled, and extracted with three 50-ml. portions of ether. The combined ethereal extracts were dried first with sodium sulfate, then with potassium hydroxide. The solution was evaporated to 30 ml., refrigerated overnight, and filtered. Light yellow crystals (3.0 g., 44% yield) melting at 120–128° were thus obtained. After recrystallizing twice from ethyl ether, once with the addition of Norit, the compound was in the form of stubby white needles which melted at 129.5–130.5°.

Anal. Calc'd for $C_{12}H_{10}N_2$: C, 79.09; H, 5.53; N, 15.44.

Found: C, 79.37; H, 5.55; N, 15.13.

2-Methyl-7,8,9,10-tetrahydro-4,7-phenanthroline. Sodium (2.0 g., 0.087 mole) was dis-

solved in 200 ml. of absolute ethanol. 1,3-Dichloro-2-methyl-4,7-phenanthroline (7.10 g., 0.0270 mole) was added followed by 2 ml. of Raney nickel sludge. The suspension was shaken in an atmosphere of hydrogen under the initial pressure of 44 p.s.i. After 19 hours, 3.1 mole-equivalents of hydrogen had been absorbed; shaking another 4 hours did not result in any further pressure drop. The solids were removed, and the solution was made exactly neutral by the careful addition of concentrated hydrochloric acid. After filtering, the solution was evaporated to 40 ml., and 160 ml. of water was added. The solution was then refrigerated overnight. The yellow solid which precipitated was filtered off and washed with 20% aqueous ethanol, these washings being added to the filtrate, which was set aside for later use. After vacuum-drying, the product weighed 1.91 g. (36%) and melted at 180–193°. Yellow cubes of m.p. 197–199° were obtained after three recrystallizations from benzene.

Anal. Calc'd for $C_{13}H_{14}N_2$: N, 14.13. Found: N, 14.19.

The *acetyl derivative* was prepared as before. After recrystallizing twice from 95% ethanol, white plates were obtained which softened at 190° and melted at 196–197.5°.

2-Methyl-5,6-dihydro-4,7-phenanthroline. This dihydro derivative was produced concurrently with 2-methyl-7,8,9,10-tetrahydro-4,7-phenanthroline by the catalytic hydrogenation described above. The combined filtrate and washings obtained after separation of the tetrahydro compound were boiled, keeping the volume constant by the addition of water, until the temperature of the escaping vapor indicated the absence of ethanol. The oil which formed on evaporation solidified on cooling, and was filtered, washed with water, and vacuum-dried. This yellow-grey solid (2.92 g.) was recrystallized from 350 ml. of water; after vacuum-drying, the white cotton-like fibers (m.p. 85–88°) weighed 2.05 g. (39% yield). Another recrystallization from water raised the m.p. to 89.5–90.5°.

Anal. Calc'd for $C_{13}H_{12}N_2$: N, 14.28. Found: N, 14.12.

The *picrate* formed slender yellow needles from ethanol, m.p. 210–213° with decomposition.

Proof of structure of 2-methyl-7,8,9,10-tetrahydro-4,7-phenanthroline. 2-Methyl-7,8,9,10-tetrahydro-4,7-phenanthroline (554 mg., 2.79 millimoles) was dissolved in 75 ml. of hot water containing 0.3 ml. of conc'd sulfuric acid. A hot solution of potassium permanganate (5.34 g., 33.8 millimoles) and potassium hydroxide (5.2 g.) in water (150 ml.) was added. The reaction mixture was refluxed for 13 hours, and the manganese dioxide was filtered off. The filtrate was made slightly acid to litmus with nitric acid, and then heated on a steam-bath. A concentrated aqueous solution of silver nitrate was added to the hot solution, which was then cooled and filtered. The precipitated silver salt was washed with water and suspended in 100 ml. of hot (80°) distilled water. Hydrogen sulfide was bubbled through the hot solution for one hour. The suspension was filtered, and the filtrate decolorized with Norit. The solution was evaporated to *ca.* 20 ml. on the steam-bath, then vacuum-dried over potassium hydroxide. The residue was treated with hot pyridine (4 ml.), filtered, and methyl ethyl ketone (6 ml.) was added to the filtrate. A small amount of a green paste formed. The solution was decanted and cooled overnight in an ice-bath. White micro-crystals (195 mg., 33% yield) of *2,3,5-tricarboxypyridine* separated. On rapid heating this substance melted at *ca.* 194° with the evolution of a gas and the formation of a solid which melted at 320–324° with decomposition. On slow heating, melting occurred only at 320–324° with decomposition. [Weber (16) reports m.p. 323°.]

After heating the tricarboxypyridine (30 mg.) for 30 minutes at 150°, the 3,5-dicarboxypyridine which had formed was allowed to react with diazomethane in ethyl ether. The ether was evaporated, and the residue crystallized from petroleum ether cooled in a Dry Ice-acetone bath. White crystals of the *dimethyl ester* of *3,5-dicarboxypyridine* were obtained melting at 83–85°, compared to the reported value of 84–85° (17).

2-Ethyl-7,8,9,10-tetrahydro-4,7-phenanthroline. Sodium (2.5 g., 0.11 mole) was dissolved in 200 ml. of absolute ethanol. 1,3-Dichloro-2-ethyl-4,7-phenanthroline (10.0 g., 0.0361 mole) was added, followed by 2 ml. of Raney nickel sludge. The suspension was shaken in an atmosphere of hydrogen under an initial pressure of 54 p.s.i. After 12 hours 3.0 mole-equivalents of hydrogen had been absorbed; shaking another 3 hours did not result in any further

pressure drop. The solids were filtered off, and the solution was made just neutral by the careful addition of concentrated hydrochloric acid. After filtering, the ethanol was boiled off, keeping the volume constant by the addition of water. The oil which formed during the removal of the ethanol solidified on refrigeration. The solid was filtered off, and washed with water at 0°. Vacuum-drying changed this solid to a yellow oil, which was then distilled. The first fraction (b.p. 169–174°/3.5 mm.) was 3.0 g. of a pale yellow liquid which was put aside for later use. The second fraction (b.p. 184–187°/3.5 mm.) was an orange liquid which solidified on standing at room temperature (1.3 g., 17% yield). After three recrystallizations from ligroin, yellow needles were obtained (m.p. 103–105°).

Anal. Calc'd for $C_{14}H_{16}N_2$: N, 13.20. Found: N, 12.92.

The *acetyl derivative* was prepared, using the method of Wibaut (13). White needles from ligroin were obtained, m.p. 83–84.5°.

2-Ethyl-5,6-dihydro-4,7-phenanthroline. The dihydro derivative was produced concurrently with the tetrahydro derivative by the catalytic hydrogenation described above. The 3.0-g. fraction (b.p. 169–174°/3.5 mm.) obtained from the vacuum distillation of the mixture of products represented a 40% yield. This pale yellow oil was crystallized from aqueous ethanol to give white fibers of the solid hydrate (m.p. 80–82°). Vacuum-drying produced a colorless oil, d_4^{20} 1.13.

Anal. Calc'd for $C_{14}H_{14}N_2$: C, 79.96; H, 6.71; N, 13.33.
Found: C, 79.57; H, 6.69; N, 13.27.

The *picrate* formed yellow stubby needles from ethanol, m.p. 185–188°.

2-Phenyl-5,6-dihydro-4,7-phenanthroline. Sodium (2.0 g., 0.087 mole) was dissolved in 200-ml. of absolute ethanol. 1,3-Dichloro-2-phenyl-4,7-phenanthroline (7.0 g., 0.0215 mole) was added followed by 2 ml. of Raney nickel sludge. The suspension was shaken in an atmosphere of hydrogen under an initial pressure of 40 p.s.i. After 26 hours 2.9 mole-equivalents of hydrogen had been absorbed; shaking another 4 hours did not result in any further pressure drop. The solids were filtered off and the solution was made just neutral by the careful addition of concentrated hydrochloric acid. After filtering, the solution was evaporated to 50 ml., and 150 ml. of water was added. A red tar separated which did not solidify after overnight refrigeration. The supernatant liquid was decanted and the residue was vacuum-dried. This residue was dissolved in 700 ml. of ethyl ether. After evaporating the solution to 200 ml. and refrigerating, 2.40 g. of a yellow solid (m.p. 161–164°) were obtained. Evaporation of the filtrate to 40 ml. and cooling produced additional material (m.p. 156–162°). The total yield was 50%. Two recrystallizations from a benzene-ligroin solution gave white rhombic crystals, m.p. 167–168°.

Evaporating the solvent from the ethereal filtrate yielded 2.89 g. of a dark orange viscous tar. No pure product could be isolated from this material.

Anal. Calc'd for $C_{18}H_{14}N_2$: N, 10.85. Found: N, 10.75.

The *picrate* formed slender yellow needles from ethanol, m.p. 211–214° with decomposition.

2-Benzyl-7,8,9,10-tetrahydro-4,7-phenanthroline. Sodium (2.0 g., 0.087 mole) was dissolved in 200 ml. of absolute ethanol. 1,3-Dichloro-2-benzyl-4,7-phenanthroline (7.40 g., 0.0218 mole) was added, followed by 3 ml. of Raney nickel sludge. The suspension was shaken in an atmosphere of hydrogen under an initial pressure of 54 p.s.i. After 6 hours 3.2 mole-equivalents of hydrogen had been absorbed; shaking another hour did not result in any further pressure drop. The solids were filtered off, and the solution made just neutral by the careful addition of concentrated hydrochloric acid. After filtering, the solution was evaporated to 100 ml., and 300 ml. of water was added. The yellow solid which precipitated after overnight refrigeration was filtered off and washed with 25% ethanol. The solid was vacuum-dried, and then refluxed with 350 ml. of ethyl ether for 15 minutes. The residue was separated and washed with ether, these washings being added to the filtrate, which was set aside for later use. The solid (m.p. 185–195°) weighed 1.30 g. (22% yield). After recrystallizing once from benzene, and twice from ethanol, highly refractive slender yellow needles were obtained, m.p. 201.5–204°.

Anal. Calc'd for $C_{19}H_{18}N_2$: N, 10.21. Found: N, 10.53.

The *acetyl derivative* was prepared, using the method of Wibaut (13). White needles were obtained from ligroin (m.p. 123.5–125°).

2-Benzyl-5,6-dihydro-4,7-phenanthroline. This dihydro derivative was produced concurrently with the above 2-benzyl-7,8,9,10-tetrahydro-4,7-phenanthroline. The ethereal solution, consisting of the combined filtrate and washings obtained after separation of the tetrahydro compound, was evaporated to 30 ml. and refrigerated overnight. After filtering and drying, the yellow fibers which had formed on cooling melted at 127–130° (62% yield). Three recrystallizations from ethyl ether gave slender white needles, m.p. 133–135°.

Anal. Calc'd for $C_{19}H_{16}N_2$: N, 10.29. Found: N, 9.99.

The *picrate* formed yellow rhombic crystals from ethanol, m.p. 200–203° with decomposition.

3,3'-Bipyridyl-2,2'-dicarboxylic acid. To a solution containing 250 mg. (1.37 millimoles) of 5,6-dihydro-4,7-phenanthroline and 250 mg. (4.47 millimoles) of potassium hydroxide in 20 ml. of water, a solution of 595 mg. (3.74 millimoles) of potassium permanganate in 12 ml. of water was added dropwise with stirring as fast as decolorization occurred (one hour), the solution being heated at first to initiate the reaction. The mixture was then digested on a steam-bath to coagulate the manganese dioxide, filtered, and neutralized with hydrochloric acid. A concentrated aqueous solution containing 4.0 g. of cupric chloride was added, and the suspension was boiled to coagulate the blue copper salt. The suspension was centrifuged, and the salt was washed thoroughly with water by successively centrifuging and decanting. It was suspended in 30 ml. of distilled water and placed in an oil-bath at 70°. Hydrogen sulfide was bubbled in slowly for one hour, and the copper sulfide then was filtered off. The solution was refluxed with Norit, filtered, and evaporated to 5 ml. on a steam-bath. After evaporating to dryness in a vacuum-desiccator, 290 mg. (78% yield) of a white solid was obtained (m.p. 210–214° with decomposition). Recrystallization from methyl ethyl ketone produced white micro-crystals melting at 214–214.5° with decomposition. Kabachnik and Reson (3), who prepared this compound in another way, reported m.p. 213.5° with decomposition.

5-Methyl-3,3'-bipyridyl-2,2'-dicarboxylic acid. A solution of 0.90 g. of potassium hydroxide in 70 ml. of water was placed in an oil-bath at 70° and stirred mechanically. A solution of 1.00 g. (5.10 millimoles) of 2-methyl-5,6-dihydro-4,7-phenanthroline in 10 ml. of pyridine was added. This was followed by the addition of a solution of 2.20 g. (13.9 millimoles) of potassium permanganate in 65 ml. of water in portions of 5 ml., each addition following the decolorization of the previous portion. The suspension was then heated on a steam-bath to coagulate the manganese dioxide, which was then filtered off. The filtrate was acidified with acetic acid and heated on a steam-bath. A concentrated aqueous solution of 3.0 g. of silver nitrate was introduced. After an hour, the silver salt had coagulated, and the suspension was cooled and centrifuged. The residue was washed thoroughly with water by successively centrifuging and decanting. The solid was suspended in 150 ml. of distilled water and placed in an oil-bath at 70°. Hydrogen sulfide was bubbled through the suspension for an hour, and the silver sulfide was filtered off. After decolorizing with Norit, the filtrate was evaporated to 10 ml. on a steam-bath, and then placed in a vacuum-desiccator. A muddy pink residue was obtained which weighed 1.16 g. After recrystallizing from methyl ethyl ketone, 0.840 g. (64% yield) of the impure acid was obtained (m.p. 180–192° with slight decomposition). After an additional three recrystallizations from the same solvent, strikingly perfect colorless cubes were obtained (m.p. 193–195° with decomposition).

Anal. Calc'd for $C_{13}H_{10}N_2O_4$: N, 10.85; C, 60.32; H, 3.90.

Found: N, 10.54; C, 60.53; H, 4.07.

5-Benzyl-3,3'-bipyridyl-2,2'-dicarboxylic acid. This compound was prepared in a similar manner as the analogous methyl derivative, starting with 1.84 g. (0.00603 mole) of 2-benzyl-5,6-dihydro-4,7-phenanthroline. After the solution containing the crude acid was evaporated to 10 ml. on a steam-bath, it was cooled in an ice-bath and centrifuged. The solution was decanted from the red oil which had formed, and the latter was extracted with 5 ml. of

boiling water, this extract being combined with the decanted portion. Upon evaporation and vacuum-drying, 500 mg. (25% yield) of a yellow solid (m.p. 120–130° with decomposition) was left as residue. After five recrystallizations from methyl ethyl ketone, white microcrystals (m.p. 180° with decomposition) were obtained.

Anal. Calc'd for $C_{19}H_{14}N_2O_4$: N, 8.38. Found: N, 7.98.

5-Phenyl-3,3'-bipyridyl-2,2'-dicarboxylic acid. This compound was prepared in a similar manner as the analogous benzyl derivative, starting with 1.55 g. (0.0060 mole) of 2-phenyl-5,6-dihydro-4,7-phenanthroline. The crude acid was a pale pink solid (1.20 g., 62% yield) melting at 126–142° with decomposition. After recrystallizing twice from methyl ethyl ketone, white rhombic crystals were obtained melting at 198–200° with decomposition.

Anal. Calc'd for $C_{18}H_{12}N_2O_4$: N, 8.75. Found: N, 8.75.

SUMMARY

1. Several 2-substituted 4,7-phenanthrolines have been prepared and identified.

2. The catalytic hydrogenation of 4,7-phenanthroline and certain 2-substituted-1,3-dichloro-4,7-phenanthrolines has been shown to give both 5,6-dihydro and 7,8,9,10-tetrahydro products.

3. Several derivatives of 6-aminoquinoline and 3,3'-bipyridyl have been synthesized and characterized.

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